

REMARKS

Claims 15 and 24-28 are pending in this application. Claims 15, 27 and 28 have been amended. Support for the amendments can be found throughout the specification. No new matter has been added.

As a preliminary matter, Applicants thank the Examiner for withdrawal of the prior claim rejections under 35 U.S.C. § 112, first paragraph, and 35 U.S.C. § 103. Applicants request reconsideration of the new rejections under 35 U.S.C. § 103 in light of the amendments and remarks below.

I. Claim Rejections under 35 U.S.C. § 103

Claims 15 and 24-28 are rejected under 35 U.S.C. § 103, as being allegedly obvious over U.S. Patent 5,902,814 (“Gordon”) in view of Jick, et al., “Statins and the risk of dementia”, *Lancet* (2000) 356:1627-31 (“Jick”) and Stalker, et al., “A new HMG-CoA reductase inhibitor, rosuvastatin, exerts anti-inflammatory effects on the microvascular endothelium: the role of mevalonic acid”, *British Journal of Pharmacology* (2001), 133:406-412 (“Stalker”). Gordon discloses spiro[1-azabicyclo[2.2.2]octane-3,5’-oxazolidine]-2’-one hydrochloride and its usefulness for treating Alzheimer’s disease, but does not disclose a combination of this compound with rosuvastatin, or a method of treating Alzheimer’s disease with said combination. To remedy this discrepancy, the Office combines Gordon with Jick and Stalker. Stalker allegedly discloses that rosuvastatin is a statin (HMG-CoA reductase inhibitor), while Jick allegedly discloses that subjects taking statins other than rosuvastatin had a reduced incidence of dementia, such as Alzheimer’s disease. On the basis of Jick, the Office alleges that statins are known to be useful for treating Alzheimer’s disease and that rosuvastatin, as a HMG-CoA reductase inhibitor (statin), would also be expected to be useful for treating Alzheimer’s disease. Therefore, the Office alleges that there is a motivation to

use a combination of spiro[1-azabicyclo[2.2.2]octane-3,5'-oxazolidine]-2'-one and rosuvastatin to treat Alzheimer's disease. Further, the Office alleges that it is *prima facie* obvious to combine two compositions which are taught in the art to be useful for the same purpose (citing *in re Kerkhoven*).

As will be appreciated, in order to establish a *prima facie* case of obviousness, the Office has the burden of showing the following three criteria: 1) a suggestion or motivation to modify or combine the reference teachings; 2) a reasonable expectation of success; and 3) the teaching of all the claim limitations by the reference(s). MPEP § 2143.

As a preliminary matter, Applicants respectfully assert that amended claim 27 is non-obvious over the cited references, because the Office has not shown a motivation to combine Jick with Gordon and Stalker to produce a combination therapy for treating Parkinson's disease. Jick is silent with respect to the ability of any statin, let alone rosuvastatin, to treat Parkinson's disease. Moreover, the Jick researchers excluded patients with a history of Parkinsonism entirely from their study (see Jick, page 1628, first column). Without a suggestion that statins can be used to treat Parkinson's disease, one of ordinary skill in the art would not be motivated to combine the Gordon compounds with a statin in order to treat Parkinson's disease, as recited in claim 27. Accordingly, Applicants respectfully assert that the Office has not carried its *prima facie* burden to show a motivation to combine the references and request that the rejection of claim 27 be withdrawn.

Similarly, amended claim 28 is also non-obvious over the cited references, because the Office has not shown a motivation to combine Jick with Gordon and Stalker to produce a combination therapy for treating Alzheimer's disease.. While Jick does disclose that subjects taking statins other than rosuvastatin had a lower risk of developing dementia, the reference does not disclose whether subjects taking statins had a lower risk of developing dementia stemming from Alzheimer's disease, rather than some other cause. Moreover, the Jick

researchers were unable to establish whether the reduced incidence in dementia could actually be attributed to the administration of a statin. For example, the Jick researchers observe “it is possible that patients who received statins were selected with regard to the level of education, socioeconomic status, and cholesterol, which themselves may be linked to dementia” and that “many observational studies provide results which are not causal” (Jick, page 1629, second column). Hence, the unsubstantiated study in Jick does not teach that any statin, let alone rosuvastatin, is **known** to treat Alzheimer’s disease. Further, as it is silent to the alleviation of the symptoms of Alzheimer’s disease, Jick is irrelevant to claim 28, which is recites a method of treating Alzheimer’s disease, rather than a method of preventing Alzheimer’s disease. Without a suggestion that statins can be used to **treat** Alzheimer’s disease, one of ordinary skill in the art would not be motivated to combine the Gordon compounds with a statin in order to treat Alzheimer’s disease, as recited in claim 28. For all of the reasons, Applicant respectfully asserts that claim 28 is not obvious over the cited references and requests that the rejection be withdrawn.

With respect to the remaining claims, the Office has not carried its *prima facie* burden to show a motivation to combine the reference teachings. In the case cited by the Office, *in re Kerkhoven*, the combination of two substances to produce a spray-dried detergent was *prima facie* obvious based on the fact that both were **known** as conventional spray-dried detergents. In the present case, however, the Office has not shown that statins are **known** to be useful for treating Alzheimer’s disease, or, indeed, any type of dementia. As stated above, Jick does not disclose whether subjects taking statins had a lower risk of developing dementia stemming from Alzheimer’s disease, rather than some other cause. Moreover, the Jick researchers were unable to conclude whether the reduced incidence in dementia could actually be attributed to the administration of a statin, observing that conclusions based on observational studies such as that in Jick may be “spurious” and pointing out the need for

substantiation (Jick, page 1629, second column, and page 1630, second column). Since Jick does not teach that administration of a statin is **known** to reduce the incidence of Alzheimer's disease or dementia, it is not *prima facie* obvious to combine the teachings of Gordon, Jick, and Stalker. Further, without a teaching that a statin would be useful for treating the same disorders as the $\alpha 7$ -nAChR agonists of claim 15, there is no motivation to combine these agonists with any statin, let alone rosuvastatin. Accordingly, Applicants respectfully assert that all of the requirements of 35 U.S.C. § 103 have been met and request that the claim rejections be withdrawn.

Claims 15 and 24-28 are rejected under 35 U.S.C. § 103, as being allegedly obvious over International Patent Publ. No. WO 98/54189 ("Peters") in view of Jick and Stalker. Peters allegedly discloses a genus of compounds encompassing (2'R)-5'-(3-furanyl)spiro[1-azabicyclo[2.2.2]octane-3,2'-(3'H)-furo[2,3-b]pyridine] and their use in treating Alzheimer's and Parkinson's disease. For reasons similar to those summarized above, the Office concludes that it would be *prima facie* obvious to combine (2'R)-5'-(3-furanyl)spiro[1-azabicyclo[2.2.2]octane-3,2'-(3'H)-furo[2,3-b]pyridine] with rosuvastatin to treat Alzheimer's disease. As summarized above, Jick does not teach that any statin, let alone rosuvastatin, is known to be useful to treat Parkinson's disease, Alzheimer's disease, or dementia. As such there is no motivation to combine Jick with Peters and Stalker. Accordingly, Applicants respectfully assert that the Office has not carried its *prima facie* burden and request that the claim rejections be withdrawn.

Claims 15 and 24-28 are rejected under 35 U.S.C. § 103, as being allegedly obvious over U.S. Application No. US2003/0018042 ("Eifion") in view of Jick and Stalker. Peters allegedly discloses (2'R)-5'-(3-furanyl)spiro[1-azabicyclo[2.2.2]octane-3,2'-(3'H)-furo[2,3-b]pyridine] and its use in treating Alzheimer's and Parkinson's disease. For reasons similar to those summarized above, the Office concludes that it would be *prima facie* obvious to

combine (2'R)-5'-(3-furanyl)spiro[1-azabicyclo[2.2.2]octane-3,2'-(3'H)-furo[2,3-b]pyridine] with rosuvastatin to treat Alzheimer's disease. As summarized above, Jick does not teach that any statin, let alone rosuvastatin, is known to be useful to treat Parkinson's disease, Alzheimer's disease, or dementia. As such there is no motivation to combine Jick with Eifion and Stalker. Applicants respectfully assert that the Office has not carried its *prima facie* burden and request that the claim rejections be withdrawn.

II. Conclusion

Applicants respectfully request reconsideration of the rejections and objections of record in light of the above comments. Further, early reconsideration and allowance of all pending claims is respectfully requested.

The Commissioner is hereby authorized to debit any fee due or credit any overpayment to deposit account 50-0436.

Respectfully submitted,

/Susanne H. Goodson/
Susanne H. Goodson, Ph.D., Reg. No. 58,450

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PEPPER HAMILTON LLP
IP Docketing
50th Floor
500 Grant Street
Pittsburgh, PA 15219-2502
(610) 640-7854 (Telephone)
(412) 281-0717 (Facsimile)